

Amendments to the Specification

Please replace the "Sequence Listing" filed on January 27, 2004 (sheets 1/3 through 3/3) with the Substitute "Sequence Listing" (sheets 1/3 through 3/3) comprising SEQ ID NOs.:1-6 filed concurrently herewith.

Please replace the paragraph at page 3, line 24 through page 4, line 26 with the following amended paragraph:

One example of an NPAR agonist is a thrombin peptide derivative, i.e., a polypeptide with less than about fifty amino acids, preferably less than about thirty-three amino acids and having sufficient homology to the fragment of human thrombin corresponding to prothrombin amino acids 508-530 (~~Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val: SEQ ID NO.: 1~~) (Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val: SEQ ID NO.: 1) that the polypeptide activates NPAR. The thrombin peptide derivatives described herein preferably have between about 14 and 23 amino acids, more preferably between about 19 and 23 amino acids. Optionally, the thrombin peptide derivatives described herein can be amidated at the C-terminus and/or acylated at the N-terminus.

In one embodiment, the thrombin peptide derivative being administered to the chronic dermal skin ulcer has the following amino acid sequence: ~~R1-Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-R2: SEQ ID NO.: 5~~ R1-Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-R2: SEQ ID NO.: 5. R1 is -H or R3-C(O)-; R2 is -OH or -NR₄R₅; R3 is -H or C1-C6 alkyl group (preferably -CH₃); and R4 and R5 are independently -H, C1-C6 alkyl group or, taken together with the nitrogen atom to which they are bonded, are a non-aromatic heterocyclic group such a piperidinyl, morpholinyl, thiomorphinyl or pyrrolidinyl (preferably R4 and R5 are both -H). Preferably R1 is -H and R2 is -NH₂; or R1 is -H and R2 is -OH. Alternatively, the thrombin peptide derivative being administered to the chronic dermal skin ulcer has the amino acid sequence of SEQ ID NO.: 3: ~~R1-Asp-Asn-Met-Phe-Cys-Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-Asp-Ser-Gly-Gly-Pro-Phe-Val-Met-Lys-Ser-Pro-Phe-R2~~ R1-Asp-Asn-Met-Phe-Cys-Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-Glu-Gly-

Asp-Ser-Gly-Gly-Pro-Phe-Val-Met-Lys-Ser-Pro-Phe-R2. R1 and R2 are as described above. It is understood, however, that zero, one, two or three amino acids at positions 1-9 and 14-23 in the thrombin peptide derivative can differ from the corresponding amino acid in SEQ ID NO.: 5. It is also understood that zero, one, two or three amino acids at positions 1-14 and 19-33 in the thrombin peptide derivative can differ from the corresponding amino acid in SEQ ID NO.: 3. Preferably, the amino acids in the thrombin peptide derivative which differ from the corresponding amino acid in SEQ ID NO.: 3 or SEQ ID NO.: 5 are conservative substitutions, and are more preferably highly conservative ~~substitutions~~ substitutions. Alternatively, an *N*-terminal truncated fragment of the thrombin peptide derivatives having at least fourteen amino acids or a *C*-terminal truncated fragment of the thrombin peptide derivative having at least eighteen amino acids can be contacted with the chronic dermal skin ulcer.

Please replace the paragraph at page 5, lines 12 through 12 with the following amended paragraph:

A preferred thrombin peptide derivative for use in the disclosed method has the amino acid sequence of SEQ ID NO.: 2: ~~R1-Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-X₁-Gly-Asp-Ser-Gly-Gly-Pro-X₂-Val-R2~~ R1-Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-X₁-Gly-Asp-Ser-Gly-Gly-Pro-X₂-Val-R2. R1 and R2 are as described above. Another preferred thrombin peptide derivative for use in the disclosed method has the amino acid sequence of SEQ ID NO.: 4: ~~R1-Asp-Asn-Met-Phe-Cys-Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-X₁-Gly-Asp-Ser-Gly-Gly-Pro-X₂-Val-Met-Lys-Ser-Pro-Phe-R2~~ R1-Asp-Asn-Met-Phe-Cys-Ala-Gly-Tyr-Lys-Pro-Asp-Glu-Gly-Lys-Arg-Gly-Asp-Ala-Cys-X₁-Gly-Asp-Ser-Gly-Gly-Pro-X₂-Val-Met-Lys-Ser-Pro-Phe-R2. X₁ is Glu or Gln; X₂ is Phe, Met, Leu, His or Val; and R1 and R2 are as described above. Alternatively, *N*-terminal truncated fragments of these preferred thrombin peptide derivatives, the *N*-terminal truncated fragments having at least fourteen amino acids or *C*-terminal truncated fragments of these preferred thrombin peptide derivative, the *C*-terminal truncated fragments having at least eighteen amino acids, can also be used in the disclosed method.